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The STIC Search Report

STIC Search Report
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STIC Database Tracking Number: 114949

TO: David Lukton Location: REM-3C70 Art Unit: 1653 February 24, 2004 Case Serial Number: 09/945237	From: P. Sheppard Location: Remsen Building Phone: (571) 272-2529 sheppard@uspto.gov

Search Notes

114949

SEARCH REQUEST FORM
(STIC)

Requestor's Name: David Lukton   Examiner number: 71263   Date: 2/23/04

Art Unit: 1653   Phone number: 571-272-0952   Serial Number: 09/945237

Mail Box: 3-C-70   Examiner Rm: 3-B-75   Results format: paper

* * * * * * * * * * * * * *

Title of Invention: Novel cyclic tetrapeptide derivatives and pharmaceutical uses thereof

Applicants: NISHINO, NORIKAZU; YOSHIDA, MINORU; HORINOUCHI, SUEHARU; KOMATSU, YASUHIKO

Earliest Priority Date: 3/2/99

* * * * *

Applicants are claiming the compounds according to each of the two formulas on the attached sheet.

R^1 = C_1 - C_5 alkylene

R^2 = C_1 - C_5 alkylene

R^3 = C_1 - C_5 alkylene

R^{11} = hydrogen, alkyl, arylalkyl, cyclohexylalkyl, cyclopentylalkyl

R^{12} = hydrogen, alkyl, arylalkyl, cyclohexylalkyl, cyclopentylalkyl

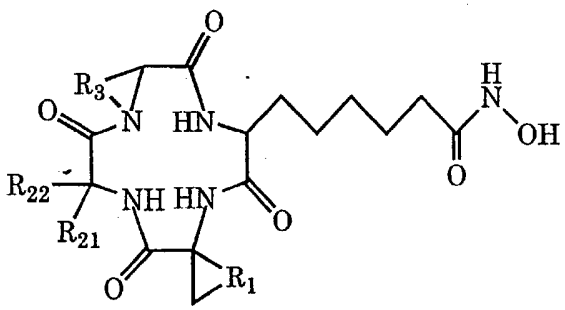
R^{21} = hydrogen, alkyl, arylalkyl, cyclohexylalkyl, cyclopentylalkyl

R^{22} = hydrogen, alkyl, arylalkyl, cyclohexylalkyl, cyclopentylalkyl

****

STAFF USE ONLY   **Type of Search**   **Vendors and cost where applicable**

09/945,237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R22
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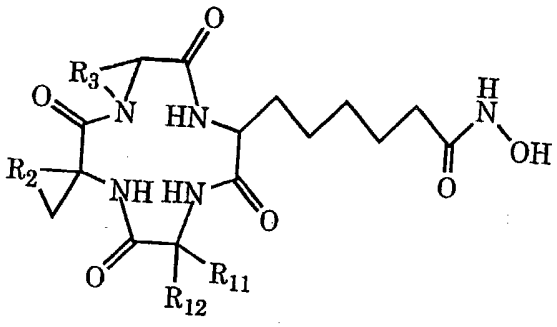
R21
O
R1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R2
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R11
R12

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 24 Feb 2004  VOL 140 ISS 9
FILE LAST UPDATED: 23 Feb 2004  (20040223/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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=> d stat que l11
L1              STR
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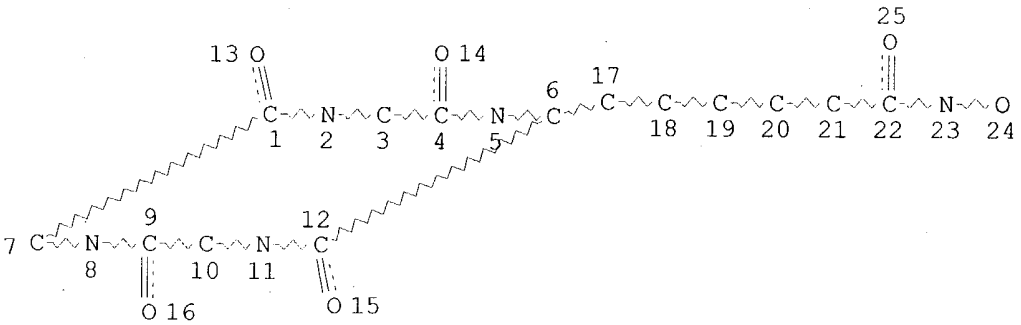


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
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L8              STR
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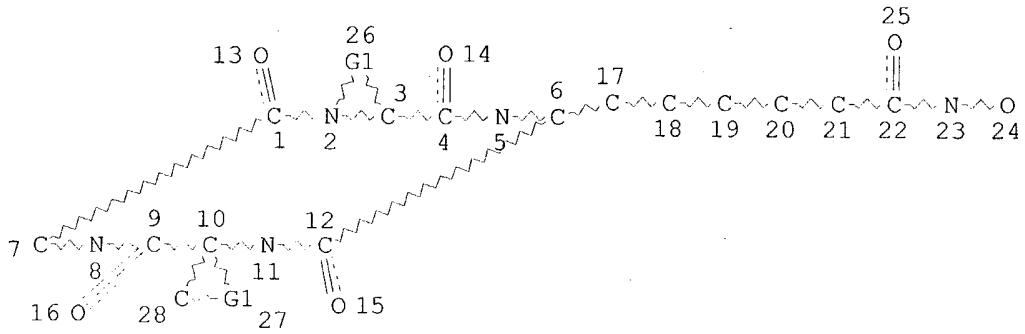

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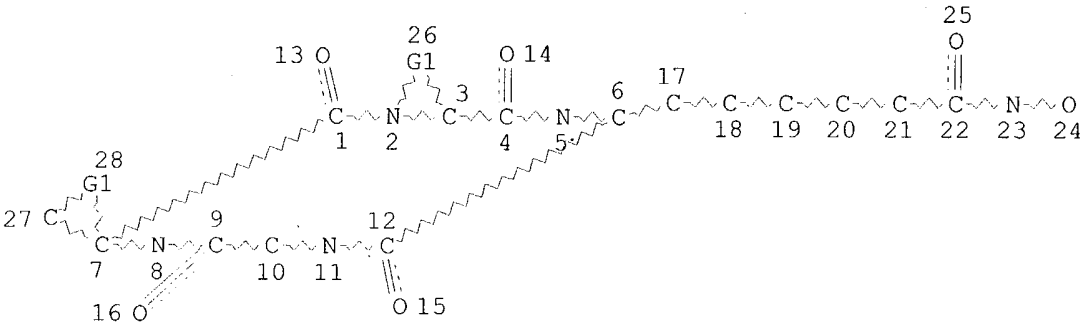
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L9 STR



REP G1=(1-5) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L10 7 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 OR L9
L11 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L10

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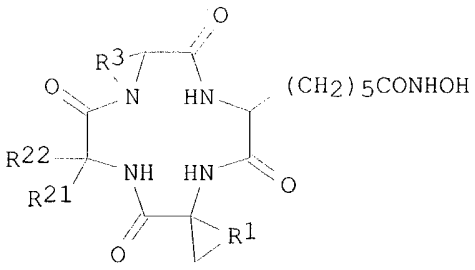
=> d ibib abs hitrn l11 1

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:628159 HCAPLUS
DOCUMENT NUMBER: 133:223052
TITLE: Preparation of novel cyclic tetrapeptide derivatives

and use thereof as drugs
INVENTOR(S): Nishino, Norikazu; Yoshida, Minoru; Horinouchi, Sueharu; Komatsu, Yasuhiko
PATENT ASSIGNEE(S): Japan Energy Corporation, Japan
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052033	A1	20000908	WO 2000-JP1141	20000228
W: AU, CA, NO, NZ, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2000256397	A2	20000919	JP 1999-53851	19990302
NZ 513983	A	20010928	NZ 2000-513983	20000228
EP 1174438	A1	20020123	EP 2000-905381	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001004225	A	20011017	NO 2001-4225	20010831
US 2002120099	A1	20020829	US 2001-945237	20010831
ZA 2001007320	A	20020904	ZA 2001-7320	20010904

PRIORITY APPLN. INFO.: JP 1999-53851 A 19990302
WO 2000-JP1141 W 20000228
OTHER SOURCE(S): MARPAT 133:223052
GI



I

AB Cyclic tetrapeptide derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof (wherein R21 and R22 are each independently hydrogen, linear C1-6 alkyl to which a nonarom. cycloalkyl group or an optionally substituted arom. ring may be bonded, or branched C3-6 alkyl to which a nonarom. cycloalkyl group or an optionally substituted arom. ring may be bonded; and R1 and R3 are each independently linear C1-5 alkylene which may have a C1-6 side chain, and the side chain may form a fused ring structure on the alkylene chain) are prepd. Also claimed are histone deacetylase inhibitors, MHC class I mol. expression promoters and anticancer drug compns., contg. as the active ingredient the above tetrapeptide derivs. or pharmaceutically acceptable salts thereof. Thus, cyclo(-L-Asu(NHOH)-2Ain-L-Phe-D-Pro-) (2Ain = 2-aminoindane-2-carboxylic acid residue), which was prepd. by the soln. phase method, in vitro at 1.29 nM doubled the amt. of MHC class I mol. expressed on the surface of B16/BL6 cells and also showed IC50 of 0.980 nM against histone deacetylase.

IT **291312-79-3P 291312-80-6P 291312-81-7P**

291312-83-9P 291312-84-0P 291312-85-1P
291312-86-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel cyclic tetrapeptide derivs. as histone deacetylase inhibitors, MHC class I mol. expression promoters, and anticancer agents)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
=> fil caold
FILE 'CAOLD' ENTERED AT 16:58:28 ON 24 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L12 0 L10

=> fil reg
FILE 'REGISTRY' ENTERED AT 16:58:38 ON 24 FEB 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 FEB 2004 HIGHEST RN 653563-64-5
DICTIONARY FILE UPDATES: 23 FEB 2004 HIGHEST RN 653563-64-5

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
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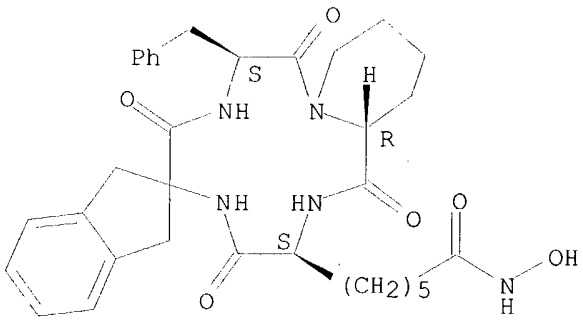
=> d ide can l10 tot

L10 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291312-86-2 REGISTRY
CN Spiro[2H-indene-2,6'-[6H]pyrido[1,2-a][1,4,7,10]tetraazacyclododecine]-3'-hexanamide, 1,1',2',3,3',4',5',7',8',9',10',12',13',14',15',15'a-hexadecahydro-N-hydroxy-1',4',7',10'-tetraoxo-9'-(phenylmethyl)-, (3'S,9'S,15'aR)- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C33 H41 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



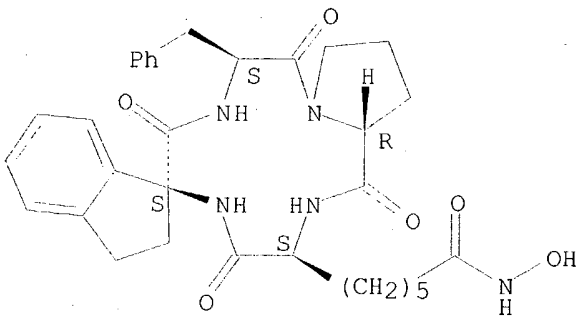
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L10 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291312-85-1 REGISTRY
CN Cyclo[(1S)-1-amino-2,3-dihydro-1H-indene-1-carbonyl-L-phenylalanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H39 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

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RN 291312-84-0 REGISTRY
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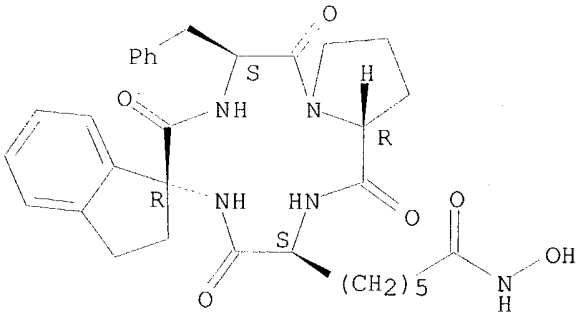
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H39 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

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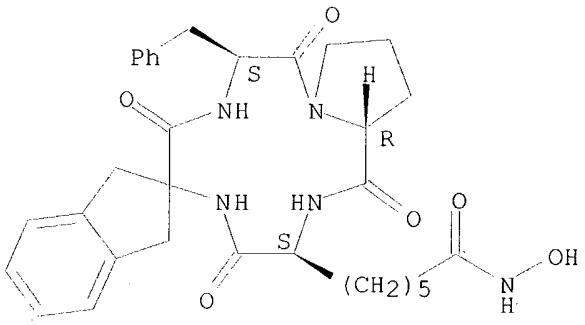
RN 291312-83-9 REGISTRY
CN Cyclo[2-amino-2,3-dihydro-1H-indene-2-carbonyl-L-phenylalanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H39 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



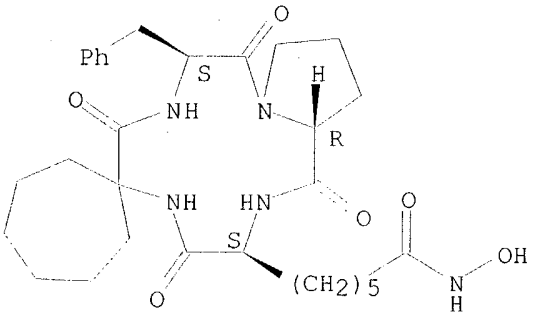
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L10 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291312-81-7 REGISTRY
CN Cyclo[1-aminocycloheptanecarbonyl-L-phenylalanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C30 H43 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



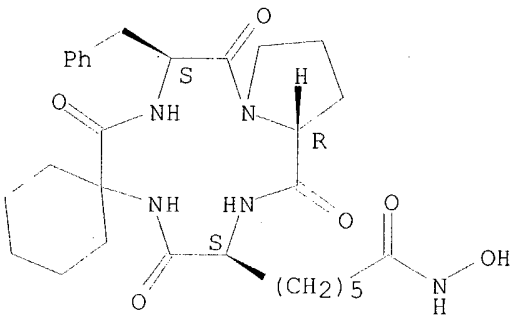
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L10 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291312-80-6 REGISTRY
CN Cyclo[1-aminocyclohexanecarbonyl-L-phenylalanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H41 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L10 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
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FS PROTEIN SEQUENCE; STEREOSEARCH
MF C28 H39 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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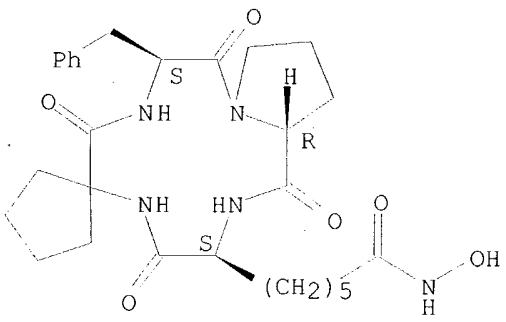

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

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FILE COVERS 1907 - 24 Feb 2004  VOL 140 ISS 9
FILE LAST UPDATED: 23 Feb 2004  (20040223/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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=>

=> d stat que l15 nos
L1             STR
L3            68 SEA FILE=REGISTRY SSS FUL L1
L8             STR
L9             STR
L10            7 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 OR L9
L11            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10
L13           61 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 NOT L10
L14           20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13
L15           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 NOT L11


=>
=>

=> d ibib abs hitrn l15 1-19

L15  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:80835  HCAPLUS
TITLE:                    Stents capable of controllably releasing histone
                          deacetylase inhibitors
INVENTOR(S):              Tseng, Xufan; Xu, Shuyun
PATENT ASSIGNEE(S):       Advanced Stent Technologies, Inc., USA
SOURCE:                   PCT Int. Appl., 73 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2004009771      A2   20040129      WO 2003-US22449  20030718
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-397780P P 20020724
US 2002-402086P P 20020809

AB A stent device includes a stent body and one or more HDAC inhibitor depot(s) provided on or in the stent body, the depot(s) capable of controllably releasing HDAC inhibitor(s). Methods of using the stents in treating and/or preventing restenosis are provided. A delivery system including the stent device and a methods of using the delivery system in treating and/or preventing restenosis are also provided. Kits comprising stents are provided. Trichostatin A inhibited human aortic SMC proliferation in vitro in a dose-dependent manner.

IT **586342-97-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stents capable of controllably releasing histone deacetylase inhibitors)

L15 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:855790 HCAPLUS
DOCUMENT NUMBER: 139:345907
TITLE: Combination therapy for the treatment of cancer using histone deacetylase inhibitors and radiotherapy
INVENTOR(S): Sgouros, George; Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard A.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003088954	A1	20031030	WO 2003-US11812	20030415

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004018968 A1 20040129 US 2003-413422 20030415

PRIORITY APPLN. INFO.: US 2002-373033P P 20020415
OTHER SOURCE(S): MARPAT 139:345907

AB The present invention relates to a method for the treatment of cancer in a patient in need thereof. The method comprises administering to a patient in need thereof a first amt. of a histone deacetylase inhibitor in a first treatment procedure, and a second amt. or dose of radiation in a second treatment procedure. The first and second treatments together comprise a therapeutically effective amt. The combination of the HDAC inhibitor and radiation therapy is therapeutically synergistic.

IT **618056-29-4**, CHAP
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for treatment of cancer using histone deacetylase inhibitors and radiotherapy)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678618 HCAPLUS
DOCUMENT NUMBER: 139:207775
TITLE: Method of treating TRX mediated diseases by administering histone deacetylase inhibitors
INVENTOR(S): Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard A.; Butler, Lisa M.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070188	A2	20030828	WO 2003-US4924	20030214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003235588	A1	20031225	US 2003-369094	20030214

PRIORITY APPLN. INFO.: US 2002-357383P P 20020215
OTHER SOURCE(S): MARPAT 139:207775
AB The invention provides a novel method for treating and/or preventing thioredoxin (TRX)-mediated diseases and conditions, by administering to a subject in need of such treatment a therapeutically effective amt. of a histone deacetylase (HDAC) inhibitor or a pharmaceutically acceptable salt or hydrate thereof. The HDAC inhibitor can alter the expression of a thioredoxin-binding-protein (e.g. TBP-2), which in turn can lead to an altered TRX/thioredoxin-binding-protein cellular binding interaction, resulting in an increase or decrease in the level or activity of cellular TRX, for example the expression level or reducing activity of TRX. Thus the invention relates to the use of HDAC inhibitors in a method of preventing and/or treating a wide variety of thioredoxin (TRX)-mediated diseases and conditions, such as inflammatory diseases, allergic diseases, autoimmune diseases, diseases assocd. with oxidative stress or diseases characterized by cellular hyperproliferation.
IT **586342-97-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of histone deacetylase inhibitors for preventing/treating thioredoxin (TRX) mediated diseases or conditions assocd. with inflammation and cellular hyperproliferation)

L15 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:551539 HCAPLUS

DOCUMENT NUMBER: 139:117688
TITLE: Preparation of cyclic tetrapeptides as histone deacetylase inhibitors
INVENTOR(S): Satoh, Shigeki; Urano, Yasuharu; Osoda, Kazuhiko; Hosaka, Mitsuru; Sawada, Kozo; Inoue, Takayuki; Mori, Hiroaki; Takagaki, Shoji; Fujimura, Takao; Matsuoka, Hideaki; Yoshizawa, Katsuhiko
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan; et al.
SOURCE: PCT Int. Appl., 447 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057722	A2	20030717	WO 2002-JP13754	20021227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-9779 A 20011228
AU 2002-952117 A 20021010
OTHER SOURCE(S): MARPAT 139:117688
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Cyclic tetrapeptides I [R1 is H; R2 is lower alkyl, aryl, (un)substituted arylalkyl, heterocyclylalkyl, cycloalkylalkyl, alkylcarbamoylalkyl, arylcarbamoylalkyl; R3, R4 are H, (un)substituted arylalkyl or heterocyclylalkyl, cycloalkylalkyl; or R3 and R4 are linked to form lower alkylene or a condensed ring or one of R3 and R4 is linked to the adjacent nitrogen atom to form a ring; R5 is H or alkyl; X is CH2 or CH2CH2; Z is alkylene or alkenylene; R6 is CR7R8R9 or NR7R8R9, where R7 is H, halo or optionally protected hydroxy, R8 is H, halo, alkyl or Ph, and R9 is H or alkyl] or their salts were prepd. histone deacetylase inhibitors. Thus, compd. II (Bn = benzyl) was prepd. and shown to have IC50 < 100 nM and-< 50 nM, resp., for inhibition of histone deacetylase and T-cell growth.

IT **561043-75-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of cyclic tetrapeptides as histone deacetylase inhibitors)

IT **561043-74-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyclic tetrapeptides as histone deacetylase inhibitors)

L15 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509378 HCAPLUS

DOCUMENT NUMBER: 140:52743
TITLE: Hydroxamic acid analogs of naturally-occurring cyclic tetrapeptides, trapoxin, WF-3161, Cyl-1, HC-toxin and chlamydocin inhibit histone deacetylases
AUTHOR(S): Nishino, Norikazu; Tomizaki, Kin-ya; Tsukamoto, Makiko; Yoshikawa, Daisuke; Shinta, Ryuzo; Nishino, Hidekazu; Tanaka, Yuji; Kato, Tamaki; Komatsu, Yasuhiko; Nishiyama, Makoto; Furumai, Ryohei; Yoshida, Minoru
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Tobata, Kitakyushu, 804-8550, Japan
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15,-2000 (2001), Meeting Date 2000, 41-42. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Cyclic hydroxamic acid-contg. peptides (CHAPs)were designed and synthesized based on sequences of naturally occurring peptides. The CHAPs were examd. for activities in histone deacetylase inhibition and MHC class-I expression.

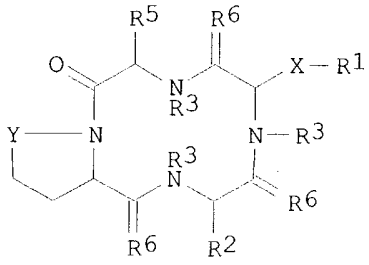
IT **221186-39-6P 221186-45-4P 221186-46-5P**
221186-60-3P 221186-64-7P 221186-66-9P
221186-70-5P 331836-53-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hydroxamic acid analogs of naturally-occurring cyclic tetrapeptides, trapoxin, WF-3161, Cyl-1, HC-toxin and chlamydocin inhibit histone deacetylases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319478 HCAPLUS
DOCUMENT NUMBER: 138:287984
TITLE: Preparation of apicidin-derived cyclic tetrapeptides
INVENTOR(S): Meinke, Peter T.; Schmatz, Dennis; Myers, Robert W.; Rattray, Sandra J.; Colletti, Steven L.; Wyvratt, Matthew J.; Fisher, Michael H.; Gurnett, Anne M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 104 pp., Cont.-in-part of U.S. Ser. No. 614,793.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078369	A1	20030424	US 2002-66451	20020131

PRIORITY APPLN. INFO.: US 1999-145329P P 19990723
US 2000-614793 A2 20000712
OTHER SOURCE(S): MARPAT 138:287984
GI



I

AB Cyclic tetrapeptide compds. I [X = CH2, CO, CHOH, alkoxy- or aryloxymethylene, etc., :CH, or not present; Y = (CH2)n, where n = 1 or 2; R1 = H, alkyl, aryl, acyl, CN, CO2H or ester, carboxamido, etc.; R2 = (un)substituted alkyl, alkenyl, or alkynyl, alkoxy, alkoxyalkyl; R3 = H, halo, OH, alkoxy, aryloxy, etc., alkyl, aryl; R5 = iso-Pr, sec-butyl; R6 = O, S, H2 (with provisos)] derived from apicidin were prepd. for therapeutic inhibition of histone deacetylase activity. Thus, treating 300 mg apicidin with 18 mg NaBH4 in MeOH and stirring 4 h at room temp. afforded carbonyl redn. product cyclo(N-O-methyl-L-Trp-L-Ile-D-Pip-L-2-amino-8-hydroxydecanoyl) (pip = pipecolic acid residue).

IT **312956-87-9P 322000-81-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of apicidin-derived cyclic tetrapeptides)

IT **312956-86-8P 322000-82-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of apicidin-derived cyclic tetrapeptides)

L15 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692467 HCAPLUS
DOCUMENT NUMBER: 138:385700
TITLE: Design of analogs of trapoxin, Cyl-1, and chlamydocin for MHC class-I molecule up-regulation
AUTHOR(S): Nishino, Norikazu; Kato, Tamaki; Komatsu, Yasuhiko; Yoshida, Minoru
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Kitakyushu, 804-8550, Japan
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 528-529. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL; ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A symposium report. Stereoisomers of trapoxin hydroxamic acid analogs were synthesized and subjected to histone deacetylase (HDAC) inhibition and major histocompatibility complex (MHC) class-I mol. up-regulating - assays. The stereoisomers of trapoxin B analogs having LDLD (7), LDLL (3) and retro-enantio DLDL (9) configurations inhibited HDAC with almost the same high potency. The isomer 7 showed nearly 200 times higher activity than the isomer 3 and 25 times higher activity than the retro-enantio analog 9 in the MHC assay. High performance liq. chromatog. retention times indicate that the hydrophobicity of the cyclic tetrapeptide framework is also necessary for MHC activity.

IT **221186-39-6P 221186-56-7P 221186-58-9P**
221186-62-5P 527705-77-7P 527705-82-4P
527705-87-9P 527705-90-4P 527705-94-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(analogs of trapoxin, Cyl-1, and chlamydocin for MHC class-I mol. up-regulation)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:431009 HCAPLUS
DOCUMENT NUMBER: 135:251418
TITLE: Cyclic hydroxamic-acid-containing peptide 31, a potent synthetic histone deacetylase inhibitor with antitumor activity
AUTHOR(S): Komatsu, Yasuhiko; Tomizaki, Kin-Ya; Tsukamoto, Makiko; Kato, Tamaki; Nishino, Norikazu; Sato, Shigeo; Yamori, Takao; Tsuruo, Takashi; Furumai, Ryohei; Yoshida, Minoru; Horinouchi, Sueharu; Hayashi, Hideya
CORPORATE SOURCE: Pharmaceuticals and Biotechnology Laboratory, Japan Energy Corporation, Saitama, 335-8502, Japan
SOURCE: Cancer Research (2001), 61(11), 4459-4466
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyclic hydroxamic-acid-contg. peptide 1 (CHAP1), designed as a hybrid of trichostatin A and trapoxin, is a lead compd. for the development of potent inhibitors of histone deacetylase (HDAC). In this study, we synthesized a series of CHAP derivs. and evaluated their biol. activities by monitoring the potency of their inhibition of HDAC activity, their ability to augment the expression of MHC class-I mols. in B16/BL6 cells, and their effect on cell proliferation. A structure-activity relation study using these three assay systems revealed several requirements of their structure for the strong inhibition of HDAC not only in the cell-free situation, but also in cells. When the structures of CHAP derivs. are represented as cyclo(-Asu(NHOH)-AA2-AA3-Pro or Pip-)n, where Asu(NHOH) and Pip are .xi.-hydroxamide-.alpha.-aminosuberic acid and pipecolic acid, resp., (a) the tetrapeptide structure (n = 1) was better than the octapeptide one (n = 2); (b) AA2 and AA3 should be hydrophobic; and (c) the combination of amino acid chirality should be LDLD for the strongest inhibition of HDAC in cells (LDLD > LLLD, LDLL > LLDL). Cyclo(-L-Asu(NHOH)-D-Tyr(Me)-L-Ile-D-Pro-) or CHAP31 was selected as one of the strongest CHAPs, and its biol. activity was characterized further. CHAP31 was much more stable in the presence of cultured cells (t1/2 > 3000 h) than trichostatin A (t1/2 = 14.7 h) or trapoxin A (t1/2 = 2.10 h). CHAP31 exhibited antitumor activity in C57BL .times. DBA/2 F1 (BD2F1) mice bearing B16/BL6 tumor cells. Furthermore, CHAP31 inhibited the growth in four of five human tumor lines implanted into nude mice. These results suggest CHAP31 to be promising as a novel therapeutic agent for cancer treatment.
IT **221186-39-6 221186-56-7 221186-57-8**
221186-58-9 221186-60-3 221186-62-5
221186-64-7 221186-66-9 221186-67-0
221186-73-8 221186-75-0 331836-53-4
362055-29-6 362055-30-9 362055-31-0
362055-32-1 362055-33-2 362055-34-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure activity studies on cyclic hydroxamic-acid-contg. peptide as potent synthetic histone deacetylase inhibitor with antitumor activity)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

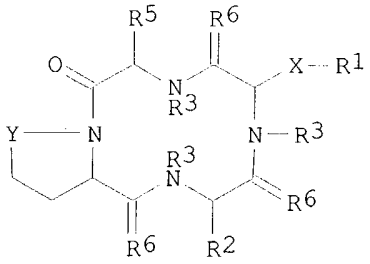
L15 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:83649 HCAPLUS
DOCUMENT NUMBER: 134:289954
TITLE: Broad spectrum antiprotozoal agents that inhibit histone deacetylase: structure-activity relationships of apicidin. Part 1
AUTHOR(S): Colletti, S. L.; Myers, R. W.; Darkin-Rattray, S. J.; Gurnett, A. M.; Dulski, P. M.; Galuska, S.; Allocco, J. J.; Ayer, M. B.; Li, C.; Lim, J.; Crumley, T. M.; Cannova, C.; Schmatz, D. M.; Wyvratt, M. J.; Fisher, M. H.; Meinke, P. T.
CORPORATE SOURCE: Merck Research Laboratories, Merck & Co., Inc., Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(2), 107-111
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apicidin, a natural product recently isolated at Merck, inhibits both mammalian and protozoan histone deacetylases (HDACs). The conversion of apicidin, a nanomolar inhibitor of HDACs, into a series of side-chain analogs that display picomolar enzyme affinity is described within this structure-activity study.
IT **312956-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiprotozoal activity and histone deacetylase inhibition by apicidin analogs)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:78233 HCAPLUS
DOCUMENT NUMBER: 134:131817
TITLE: Preparation of apicidin-derived cyclic tetrapeptides
INVENTOR(S): Meinke, Peter T.; Schmatz, Dennis; Fisher, Michael H.; Rattray, Sandra J.; Colletti, Steven L.; Wyvratt, Matthew J.; Myers, Robert W.; Gurnett, Anne M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 229 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007042	A1	20010201	WO 2000-US19627	20000719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1204411 A1 20020515 EP 2000-947507 20000719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
JP 2003505417 T2 20030212 JP 2001-511926 20000719
PRIORITY APPLN. INFO.: US 1999-145329P P 19990723
WO 2000-US19627 W 20000719
OTHER SOURCE(S): MARPAT 134:131817
GI



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AB Cyclic tetrapeptide compds. I [X = CH2, CO, CHOH, alkoxy- or aryloxymethylene, etc., :CH, or not present; Y = (CH2)n, where n = 1 or 2; R1 = H, alkyl, aryl, acyl, CN, CO2H or ester, carboxamido, etc.; R2 = (un)substituted alkyl, alkenyl, or alkynyl, (CH2)nii-O-(CH2)mii, where nii, mii = 0-7; R3 = H, halo, OH, alkoxy, aryloxy, etc., alkyl, aryl; R5 = iso-Pr, sec-butyl; R6 = O, S, H2 (with provisos)] derived from apicidin were prepd. for therapeutic inhibition of histone deacetylase activity. Thus, treating 300 mg apicidin with 18 mg NaBH4 in MeOH and stirring 4 h at room temp. afforded carbonyl redn. product cyclo(N-O-methyl-L-Trp-L-Ile-D-Pip-L-2-amino-8-hydroxydecanoyl) (pip = pipecolic acid residue).

IT **312956-87-9P 322000-81-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of apicidin-derived cyclic tetrapeptides)

IT **312956-86-8P 322000-82-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of apicidin-derived cyclic tetrapeptides)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:47667 HCAPLUS
DOCUMENT NUMBER: 134:260861
TITLE: Potent histone deacetylase inhibitors built from trichostatin A and cyclic tetrapeptide antibiotics including trapoxin
AUTHOR(S): Furumai, Ryohei; Komatsu, Yasuhiko; Nishino, Norikazu; Khochbin, Saadi; Yoshida, Minoru; Horinouchi, Sueharu
CORPORATE SOURCE: Department of Biotechnology, The University of Tokyo, Tokyo, 113-8657, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(1), 87-92
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trichostatin A (TSA) and trapoxin (TPX) are potent inhibitors of histone deacetylases (HDACs). TSA is proposed to block the catalytic reaction by

chelating a zinc ion in the active-site pocket through its hydroxamic acid group. On the other hand, the epoxyketone is suggested to be the functional group of TPX capable of alkylating the enzyme. We synthesized a novel TPX analog contg. a hydroxamic acid instead of the epoxyketone. The hybrid compd. cyclic hydroxamic acid-contg. peptide (CHAP) 1 inhibited HDAC1 at low nanomolar concns. The HDAC1 inhibition by CHAP1 was reversible as it was by TSA, in contrast to the irreversible inhibition by TPX. CHAP with an aliph. chain length of five, which corresponded to that of acetylated lysine, was stronger than those with other lengths. These results suggest that TPX is a substrate mimic and that the replacement of the epoxyketone with the hydroxamic acid converted TPX to an inhibitor chelating the zinc like TSA. Interestingly, HDAC6, but not HDAC1 or HDAC4, was resistant to TPX and CHAP1, whereas TSA inhibited these HDACs to a similar extent. HDAC6 inhibition by TPX at a high concn. was reversible, probably because HDAC6 is not alkylated by TPX. We further synthesized the counterparts of all known naturally occurring cyclic tetrapeptides contg. the epoxyketone. HDAC1 was highly sensitive to all these CHAPs much more than HDAC6, indicating that the structure of the cyclic tetrapeptide framework affects the target enzyme specificity. These results suggest that CHAP is a unique lead to develop isoform-specific HDAC inhibitors.

IT **221186-39-6 221186-45-4 221186-46-5 221186-60-3 221186-66-9 221186-70-5 331836-53-4**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(potent histone deacetylase inhibitors built from trichostatin A and cyclic tetrapeptide antibiotics including trapoxin)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:805814 HCAPLUS

DOCUMENT NUMBER: 134:42434

TITLE: Synthesis of side chain modified apicidin derivatives: potent mechanism-based histone deacetylase inhibitors

AUTHOR(S): Meinke, Peter T.; Colletti, Steven L.; Ayer, Michelle B.; Darkin-Rattray, Sandra J.; Myers, Robert W.; Schmatz, Dennis M.; Wyvratt, Matthew J.; Fisher, Michael H.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, Merck and Co., Inc., Rahway, NJ, 07065, USA

SOURCE: Tetrahedron Letters (2000), 41(41), 7831-7835 CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:42434

AB An efficient degrdn. of apicidin's ketone-contg. side chain to two common intermediates (the C7-aldehyde and the C8-Me ester) is described. From these intermediates, a series of potent mechanism-based histone deacetylase inhibitors was prepd. to facilitate biochem. studies.

IT **312956-87-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of side chain modified apicidin derivs. for use as histone deacetylase inhibitors)

IT **312956-86-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of side chain modified apicidin derivs. for use as histone deacetylase inhibitors)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:288753 HCAPLUS
DOCUMENT NUMBER: 133:164306
TITLE: Cyclic tetrapeptide hydroxamic acids related to trapoxin B inhibit histone deacetylase
AUTHOR(S): Nishino, Norikazu; Tomizaki, Kin-Ya; Mimoto, Tsutomu; Komatsu, Yasuhiko; Kim, Young Bae; Yoshida, Minoru
CORPORATE SOURCE: Institute for Fundamental Research of Organic Chemistry, Kyushu University, Fukuoka, 812-8581, Japan
SOURCE: Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 832-833. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Trapoxin B analogs, cyclic tetrapeptides contg. .alpha.-aminosuberyl, .alpha.-aminoazelayl, and .alpha.-aminopimelyl .omega.-hydroxamic acids, were prepd. and tested for inhibition of histone deacetylase.
IT **221186-39-6P 221186-56-7P 221186-58-9P 221186-59-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of trapoxin B-related cyclic tetrapeptide hydroxamic acids as histone deacetylase inhibitors)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:288752 HCAPLUS
DOCUMENT NUMBER: 133:135601
TITLE: Synthesis of cyclic tetrapeptide hydroxamic acids by the use of oxime resin
AUTHOR(S): Nishino, Norikazu; Tomizaki, Kin-Ya; Tsukamoto, Makiko; Urakawa, Toshihiro
CORPORATE SOURCE: Institute for Fundamental Research of Organic Chemistry, Kyushu University, Fukuoka, 812-8581, Japan
SOURCE: Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 830-831. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. For the synthesis of cyclic tetrapeptides, we examd. various methods using Kaiser's oxime resin, such as solid-phase synthesis and high diln. cyclization in soln., cyclization cleavage, and cyclization on the resin (SPS-CS, SPS-CC, SPS-CR methods).
IT **221186-46-5P 221186-70-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of cyclic tetrapeptide hydroxamic acids by use of oxime resin)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:353258 HCAPLUS
DOCUMENT NUMBER: 131:130254

TITLE: Synthesis of cyclic tetrapeptides containing non-natural imino acids
AUTHOR(S): Nishino, Hidekazu; Tomizaki, Kin-Ya; Kato, Tamaki; Nishino, Norikazu; Yoshida, Minoru; Komatsu, Yasuhiko
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Kitakyushu, 804-8550, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 189-192
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A symposium report. Cyl-2, WF-3161, and trapoxin A are inhibitors of the root growth of lettuce seedlings, cell growth in mouse P-388 leukemia cells, and mammalian histone deacetylase, resp. Unique amino acids (2S,9S)-2-amino-8-oxo-9,10-epoxydecanoic acid (L-Aoe) and pipecolic acid (Pip) are found within these cyclic tetrapeptide inhibitors : cyclo[L-Aoe-D-Tyr(Me)-L-Ile-L-Pip] (Cyl-2), cyclo(L-Aoe-D-Phe-L-Leu-L-Pip) (WF-3161), and cyclo(L-Aoe-L-Phe-L-Phe-D-Pip) (Trapoxin A). In order to study the effects of Pip on the inhibitory activity of these peptides toward histone deacetylase, the authors replaced it with various imino acids, such as 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic), hexamethyleneimine carboxylic acid (6Mic), and heptamethyleneimine carboxylic acid (7Mic), to obtain cyclo[L-Asu(NHOH)-D-Tyr(Me)-L-Ile-Xaa] (Xaa = Tic, 6Mic, 7Mic).

IT **221186-66-9P 221186-67-0P 221186-68-1P**
221186-69-2P 234112-50-6P 234112-51-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of imino acid-contg. cyclic tetrapeptides as inhibitors of histone deacetylase)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:353257 HCAPLUS
DOCUMENT NUMBER: 131:130253
TITLE: Synthesis and activity of Cyl-1 analogs having hydroxamic acid at side chain
AUTHOR(S): Tsukamoto, Makiko; Tomizaki, Kin-Ya; Kato, Tamaki; Nishino, Norikazu; Yoshida, Minoru; Komatsu, Yasuhiko
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Kitakyushu, 804-8550, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 185-188
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A symposium report. Trichostatin A, trapoxin A and B [cyclo(L-Aoe-L-Phe-L-Phe-D-Xaa); Aoe = (2S,9S) 2-amino-8-oxo-9,10-epoxydecanoic acid; Xaa = Pip (trapoxin A), Pro (trapoxin B)] are known as inhibitors of histone deacetylase (HDAC). Trichostatin A is a reversible inhibitor with hydroxamic acid functionality, and trapoxin A and B are irreversible inhibitors with epoxy ketone group at the side chain of Aoe. On the other hand, Cyl-1, cyclo(L-Aoe-D-Tyr(Me)-L-Ile-L-Pro), was discovered as an inhibitor of the root growth of lettuce seedlings. Since the structure of Cyl-1 resembles trapoxin B, the authors synthesized various Cyl-1 analogs where L-Aoe is substituted by amino acids contg. an hydroxamic acid in the side chain, such as L-Asu(NHOH).

IT **221186-60-3P 221186-64-7P 221186-73-8P**
221186-74-9P 234123-22-9P 234123-23-0P
234123-24-1P 234123-25-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of hydroxamic acid-contg. Cyl-1 analogs as inhibitors of histone deacetylase)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:353256 HCAPLUS
DOCUMENT NUMBER: 131:130252
TITLE: Histone deacetylase inhibitors based on trapoxin B
AUTHOR(S): Tomizaki, Kin-Ya; Kato, Tamaki; Nishino, Norikazu; Yoshida, Minoru; Komatsu, Yasuhiko
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Kitakyushu, 804-8550, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 181-184
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A symposium report. Trapoxin B is a cyclic tetrapeptide contg. a unique amino acid, (2S,9S)-2-amino-8-oxo-9,10-epoxydecanoic acid (L-Aoe), whose epoxyketone moiety is supposed to react with mammalian histone deacetylase. The authors synthesized a trapoxin B analog, in which L-Aoe is replaced with L-aminosuberic hydroxamic acid [Asu(NHOH)]. The analog strongly inhibited a histone deacetylase from mouse B16/BL6 cells. Furthermore, the positions of D-amino acids in the trapoxin B hydroxamic acid analog were changed. In addn. to L-L-L-D-form [contg. L-Asu(NHOH)], L-L-D-L-, L-D-L-L-, and L-D-L-D-isomers were synthesized. The L-D-L-L- and L-D-L-D-isomers exhibited high inhibitory activity, while L-L-D-L-isomer was inactive.
IT **221186-39-6 221186-56-7 221186-57-8**
221186-58-9 221186-59-0 221186-62-5
234429-76-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of hydroxamic analogs of trapoxin B as inhibitors of histone deacetylase)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:353220 HCAPLUS
DOCUMENT NUMBER: 131:116496
TITLE: Conformational analysis of non-natural LDLD-type Cyl-1 analog with high activity
AUTHOR(S): Kato, Tamaki; Tomizaki, Kin-Ya; Tsukamoto, Makiko; Nishino, Norikazu; Yoshida, Minoru; Komatsu, Yasuhiko
CORPORATE SOURCE: Department of Applied Chemistry, Faculty of Engineering, Kyushu Institute of Technology, Kitakyushu, 804-8550, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 41-44
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cyl-1 hydroxamic acid analogs, cyclo[-L-Asu(NHOH)-D-Tyr(Me)-L-Ile-(L- and

D-)Pro-] (Asu = aminosuberic acid), are inhibitors of histone deacetylase (HDAC). The inhibitory activities of LDLL-type and LDLD-type analogs against HDAC are almost same (IC50 = 3.3 nM). NMR expts. in DMSO-d at room temp. and mol. mechanics calcn. show that the side chain conformation of non-natural LDLD-type analog is similar to that of natural LDLL-type analog in spite of the difference in configurations. This conformational resemblance of the two analogs will explain why the inhibitory activities of these analogs are almost same.

IT **221186-60-3 221186-64-7**
RL: PRP (Properties)
(conformational anal. of LDLL- and LDLD-types of Cyl-1 hydroxamic acid analogs)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:184270 HCAPLUS
DOCUMENT NUMBER: 130:237885
TITLE: Preparation of novel cyclic tetrapeptide derivatives as histone deacetylase inhibitors and MHC class-1 molecule expression promoters
INVENTOR(S): Nishino, Norikazu; Yoshida, Minoru; Horinouchi, Sueharu; Komatsu, Yasuhiko; Mimoto, Tsutomu
PATENT ASSIGNEE(S): Japan Energy Corporation, Japan
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 9911659	A1	19990311	WO 1998-JP3893	19980901
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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AU 9888885	A1	19990322	AU 1998-88885	19980901
AU 732299	B2	20010412		
EP 1010705	A1	20000621	EP 1998-940649	19980901
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JP 3494624	B2	20040209	JP 2000-508697	19980901
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US 6399568	B1	20020604	US 2000-486783	20000301

PRIORITY APPLN. INFO.: JP 1997-237481 A 19970902
JP 1998-63270 A 19980313
WO 1998-JP3893 W 19980901

OTHER SOURCE(S): MARPAT 130:237885
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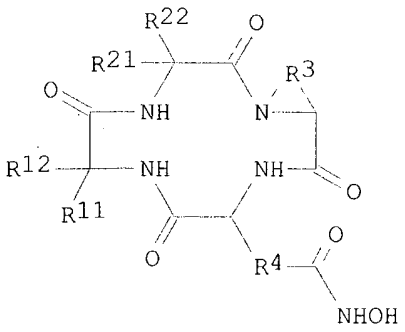

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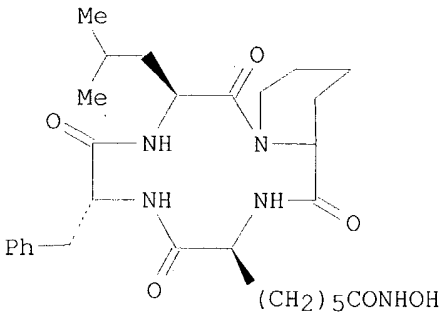

II

AB Claimed are cyclic tetrapeptide derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof and cyclic tetrapeptide compds. analogous thereto [wherein R11, R12, R21 and R22 represent each hydrogen or a monovalent group selected from linear or branched C1-6 alkyl, benzyl, 4-methoxybenzyl, 3-indolylmethyl, (N-methoxy-3-indolyl)methyl, (N-formyl-3-indolyl)methyl, etc.; R3 represents a divalent group selected from divalent linear C3-4 hydrocarbyl optionally having a branched chain added thereto or optionally substituted by a heteroatom; and R4 represents a divalent group derived from divalent linear C4-6 hydrocarbyl optionally having a branched chain added thereto]. Also claimed are histone deacetylase inhibitors, MHC class-1 mol. expression promoters, and anticancer agents contg. these cyclic tetrapeptide derivs. as the active ingredient. The hydroxamic acid side chain is responsible for the activity of MHC class-1 mol. expression promotion. These cyclotetrapeptides markedly promote the removal of cancer cells by immune cells using promotion of MHC-1 mol. expression, since they also inhibit cell proliferation and cell cycles, thereby the expansion of cancer tissues, based on histone deacetylase inhibition. They are much more reduced in undesirable side-effects such as cell proliferation inhibition and cell cycle inhibition against normal cells as compared to irreversible enzyme inhibitors, since histone deacetylase enzyme inhibition is reversible. Thus, the title peptide (II) was prepd. via deprotection of Boc-Asu(OBzl)-D-Phe-Leu-DL-Pip-OtBu (Asu = .alpha.-aminosuberic acid residue, Pip = 2-carboxypiperidine residue) (prepn. given), cyclization, and conversion of the side-chain carboxylic acid into hydroxyaminocarbonyl group. II at 3.86 nM in vitro promoted twice the expression of MHC-1 mol. in mouse melanoma B16/BL6 cells as compared to 3.35 nM for trichostatin A and showed IC50 of 12.3 nM against the proliferation of B16/BL6 cells as compared to 14.3 nM for trichostatin A.

IT **221186-39-6P 221186-44-3P 221186-45-4P**
221186-46-5P 221186-47-6P 221186-48-7P
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221186-68-1P 221186-69-2P 221186-70-5P
221186-73-8P 221186-74-9P 221186-75-0P
221186-76-1P 221186-77-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel cyclic tetrapeptide derivs. as histone deacetylase inhibitors and MHC class-1 mol. expression promoters and anticancer agents)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE LAST UPDATED:  01 May 1997 (19970501/UP)

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  now searchable from 1907-1966.  TIFF images of CA abstracts
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L16           0 L13

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STRUCTURE FILE UPDATES:   23 FEB 2004  HIGHEST RN 653563-64-5
DICTIONARY FILE UPDATES:  23 FEB 2004  HIGHEST RN 653563-64-5

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Experimental and calculated property data are now available. For more
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http://www.cas.org/ONLINE/DBSS/registryss.html

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L13  ANSWER 1 OF 61  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   618056-29-4  REGISTRY
CN   Cyclo[(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-phenylalanyl-L-
     phenylalanylprolyl] (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   CHAP
FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C31 H39 N5 O6
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

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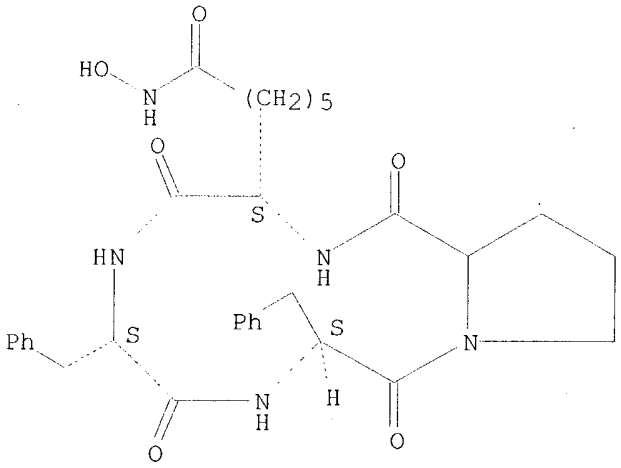


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L13  ANSWER 2 OF 61  REGISTRY  COPYRIGHT 2004 ACS on STN
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FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C31 H39 N5 O6
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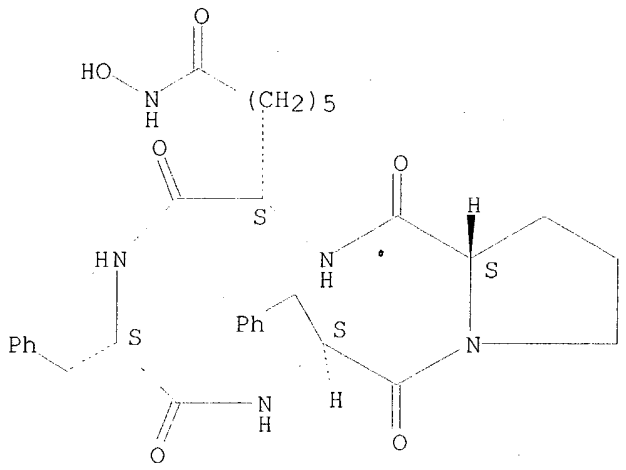

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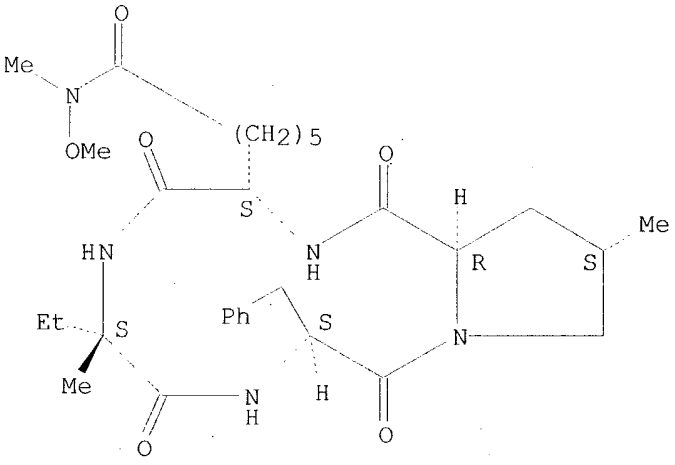
REFERENCE 1: 139:207775

L13 ANSWER 3 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 561043-75-2 REGISTRY
CN Cyclo[L-isovalyl-L-phenylalanyl-(4S)-4-methyl-D-prolyl-(2S)-2-amino-8-(methoxymethylamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C30 H45 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:117688

L13 ANSWER 5 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 527705-94-8 REGISTRY
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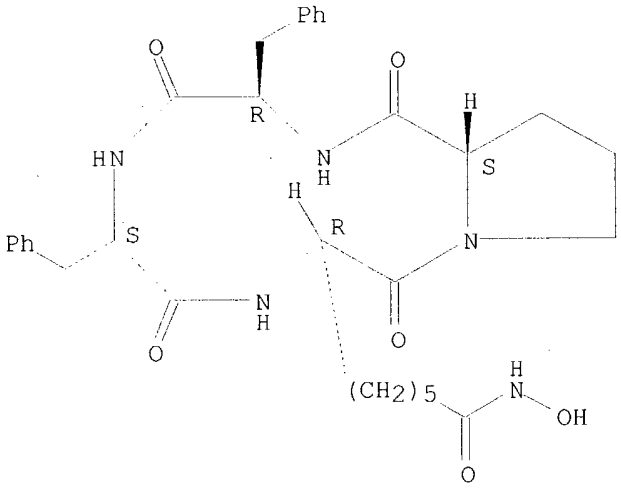
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



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REFERENCE 1: 138:385700

L13 ANSWER 10 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 362055-34-3 REGISTRY
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FS PROTEIN SEQUENCE; STEREOSEARCH
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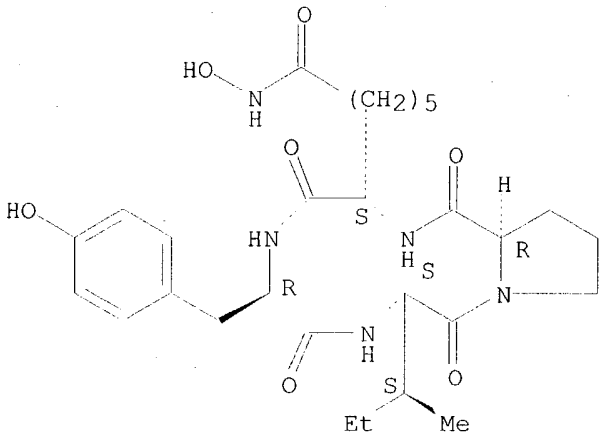
Absolute stereochemistry.



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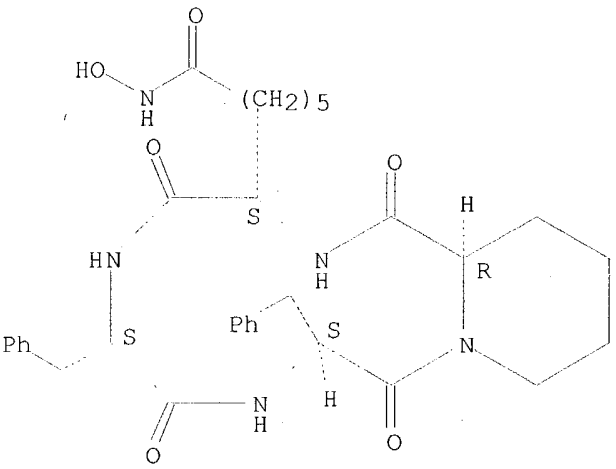
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:251418

L13 ANSWER 16 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 331836-53-4 REGISTRY
CN Cyclo[(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-phenylalanyl-L-phenylalanyl-(2R)-2-piperidinecarbonyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H41 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:52743

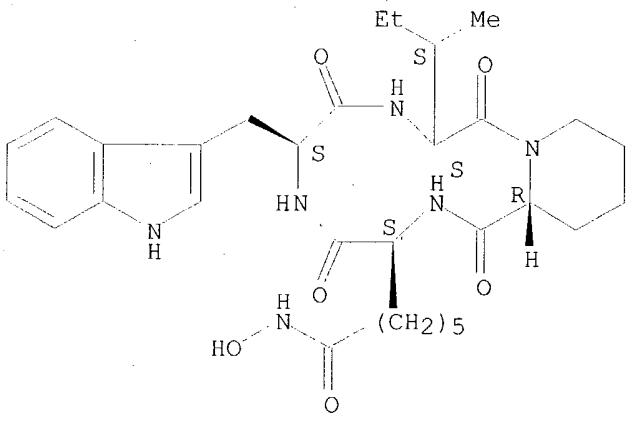
REFERENCE 2: 135:251418

REFERENCE 3: 134:260861

L13 ANSWER 17 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 322000-82-8 REGISTRY
CN Cyclo[L-isoleucyl-(2R)-2-piperidinecarbonyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-tryptophyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C31 H44 N6 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

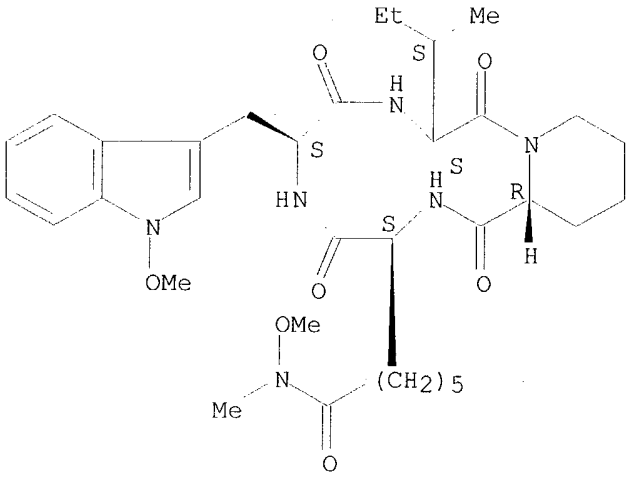
REFERENCE 1: 138:287984

REFERENCE 2: 134:131817

L13 ANSWER 19 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 312956-87-9 REGISTRY
CN Cyclo[L-isoleucyl-(2R)-2-piperidinecarbonyl-(2S)-2-amino-8-(methoxymethylamino)-8-oxooctanoyl-1-methoxy-L-tryptophyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C34 H50 N6 O7
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

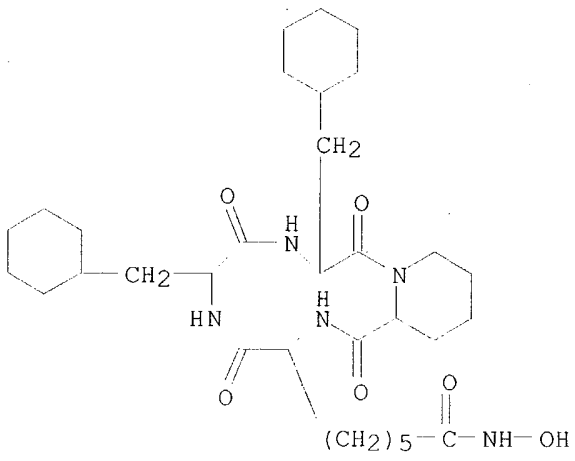
REFERENCE 1: 138:287984

REFERENCE 2: 134:131817

REFERENCE 3: 134:42434

L13 ANSWER 21 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291313-23-0 REGISTRY
CN Cyclo[3-cyclohexyl-D-alanyl-3-cyclohexyl-L-alanyl-(2R)-2-piperidinecarbonyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H53 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK



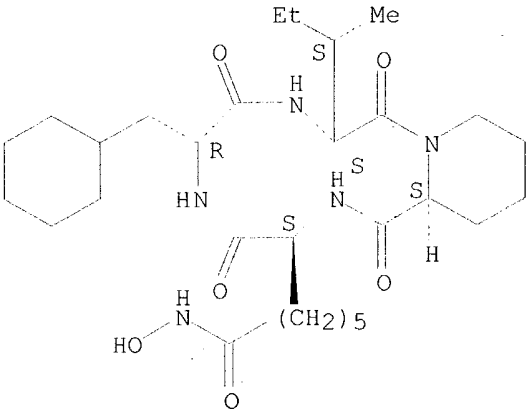
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L13 ANSWER 25 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 291312-92-0 REGISTRY
CN Cyclo[3-cyclohexyl-D-alanyl-L-isoleucyl-(2S)-2-piperidinecarbonyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H49 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

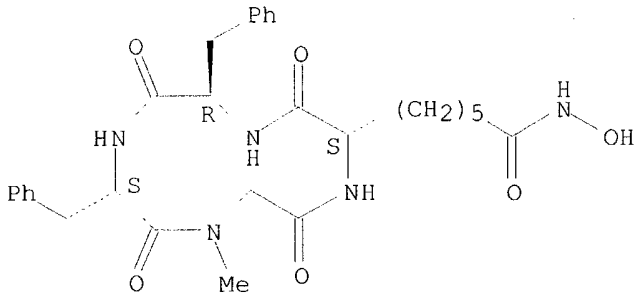


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:223052

L13 ANSWER 29 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 234429-76-6 REGISTRY
CN Cyclo[N-methylglycyl-(2S)-2-amino-8-(hydroxymethyl)-8-oxooctanoyl-D-phenylalanyl-L-phenylalanyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H37 N5 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



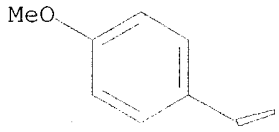
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:130252

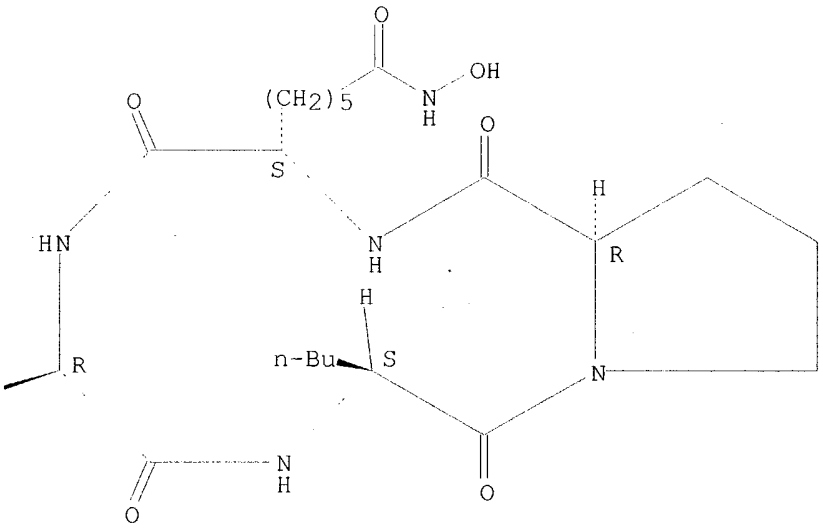
L13 ANSWER 30 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 234123-25-2 REGISTRY
CN Cyclo[L-norleucyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-O-methyl-D-tyrosyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H43 N5 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



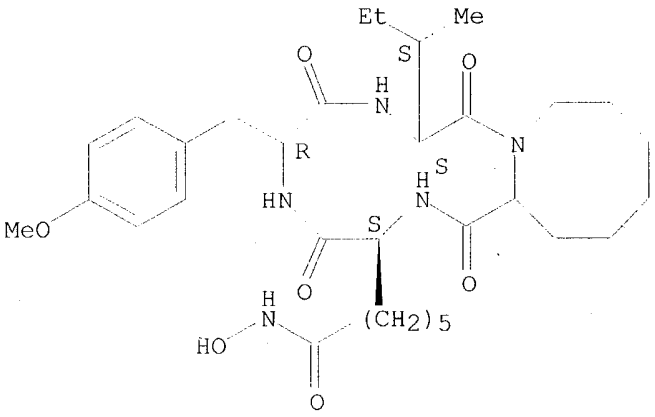
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:130253

L13 ANSWER 34 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 234112-51-7 REGISTRY
CN Cyclo[octahydro-2-azocinecarbonyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-O-methyl-D-tyrosyl-L-isoleucyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C32 H49 N5 O7
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



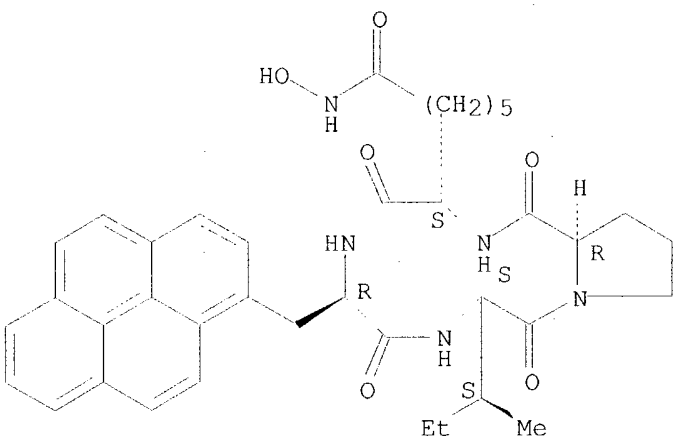
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:130254

L13 ANSWER 36 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-77-2 REGISTRY
CN Cyclo[3-(1-pyrenyl)-D-alanyl-L-isoleucyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C38 H45 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



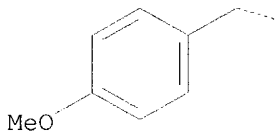
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:237885

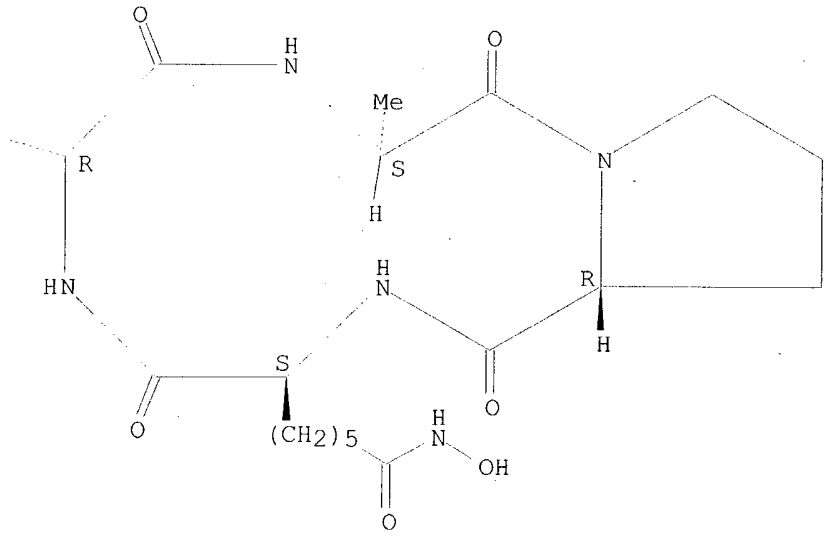
L13 ANSWER 40 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-73-8 REGISTRY
CN Cyclo[L-alanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-O-methyl-D-tyrosyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C26 H37 N5 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:251418

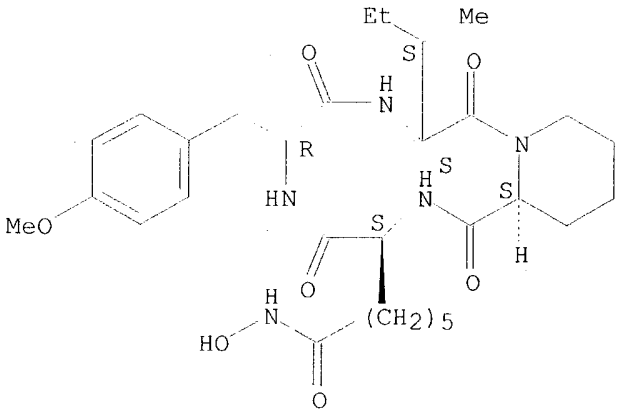
REFERENCE 2: 131:130253

REFERENCE 3: 130:237885

L13 ANSWER 45 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-66-9 REGISTRY
CN Cyclo[L-isoleucyl-(2S)-2-piperidinecarbonyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-O-methyl-D-tyrosyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C30 H45 N5 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:52743

REFERENCE 2: 135:251418

REFERENCE 3: 134:260861

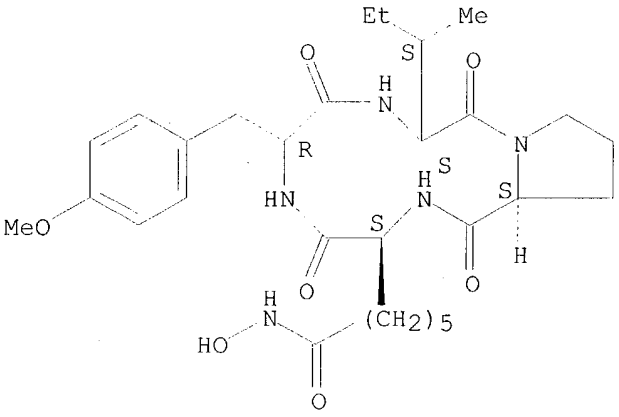
REFERENCE 4: 131:130254

REFERENCE 5: 130:237885

L13 ANSWER 50 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-60-3 REGISTRY
CN Cyclo[L-isoleucyl-L-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-O-methyl-D-tyrosyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C29 H43 N5 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:52743

REFERENCE 2: 135:251418

REFERENCE 3: 134:260861

REFERENCE 4: 131:130253

REFERENCE 5: 131:116496

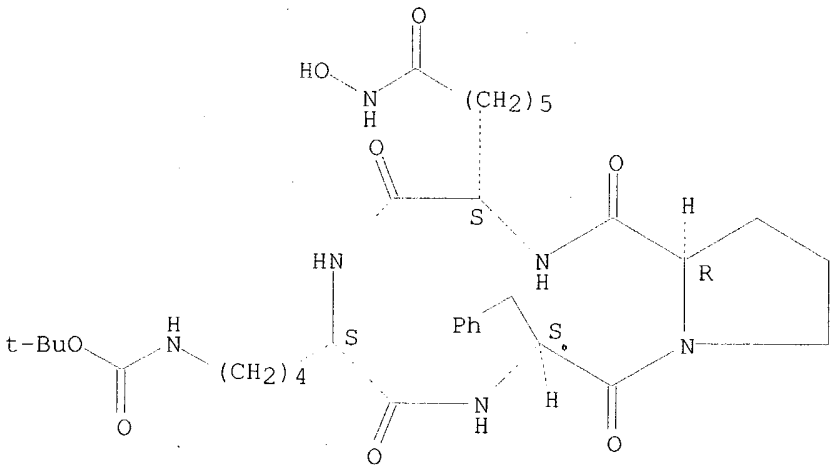
REFERENCE 6: 130:237885

L13 ANSWER 55 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-49-8 REGISTRY
CN Cyclo[N6-[(1,1-dimethylethoxy)carbonyl]-L-lysyl-L-phenylalanyl-D-prolyl-(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH

MF C33 H50 N6 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



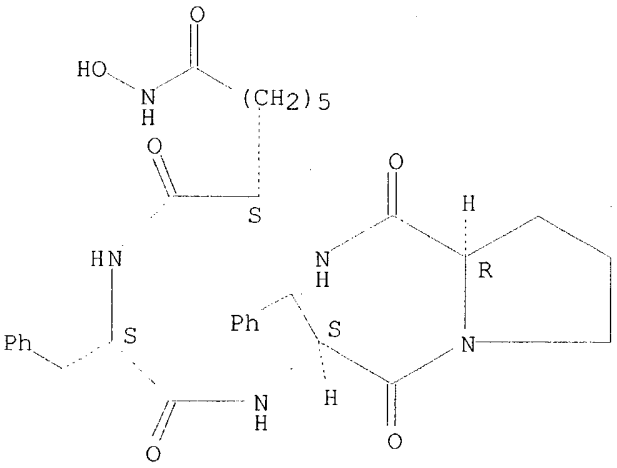
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:237885

L13 ANSWER 61 OF 61 REGISTRY COPYRIGHT 2004 ACS on STN
RN 221186-39-6 REGISTRY
CN Cyclo[(2S)-2-amino-8-(hydroxyamino)-8-oxooctanoyl-L-phenylalanyl-L-phenylalanyl-D-prolyl] (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C31 H39 N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:52743

REFERENCE 2: 138:385700

REFERENCE 3: 135:251418

REFERENCE 4: 134:260861

REFERENCE 5: 133:164306

REFERENCE 6: 131:130252

REFERENCE 7: 130:237885